

In re Application of: Shabat et al
Serial No.: 10/525,951
Filed: February 28, 2005
Office Action Mailing Date: December 10, 2008

Examiner: Trevor M. Love
Group Art Unit: 1611
Attorney Docket: 29195

In the Claims:

1. (Currently Amended) A self-immolative dendrimer comprising a cleavable trigger unit, a plurality of tail units and at least one self-immolative chemical linker linking between said trigger unit and said tail units, said trigger unit and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker self-immolates, thereby simultaneously releasing all of said tail units.

2. (Original) The self-immolative dendrimer of claim 1, wherein said tail units comprise at least two functional moieties, said at least two functional moieties being the same or different.

3. (Original) The self-immolative dendrimer of claim 1, further comprising at least one self-immolative spacer.

4. (Original) The self-immolative dendrimer of claim 3, wherein said spacer linking said trigger unit and said at least one self-immolative chemical linker.

5. (Original) The self-immolative dendrimer of claim 3, wherein said at least one spacer linking at least one of said tail units and at least one of said at least one chemical linker.

6. (Original) The self-immolative dendrimer of claim 3, wherein said trigger unit, said at least one spacer and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker and said at least one spacer self-immolate to thereby release said tail units.

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7. (Original) The self-immolative dendrimer of claim 1, wherein said cleavable trigger unit is selected from the group consisting of a photo-labile trigger unit, a chemically removable trigger unit, a hydrolysable trigger unit and a biodegradable trigger unit.

8. (Original) The self-immolative dendrimer of claim 7, wherein said biodegradable trigger unit is an enzymatically cleavable trigger unit.

9. (Original) The self-immolative dendrimer of claim 2, wherein said functional moieties comprise at least one therapeutically active agent.

10. (Original) The self-immolative dendrimer of claim 2, wherein said functional moieties comprise at least two therapeutically active agents.

11. (Original) The self-immolative dendrimer of claim 2, wherein said at least two therapeutically active agents are synergistic.

12. (Original) The self-immolative dendrimer of claim 2, wherein said functional moieties comprise at least one diagnostic agent.

13. (Previously Presented) The self-immolative dendrimer of claim 9, wherein each of said therapeutically active agents is selected from the group consisting of an anti-proliferative agent, an anti-inflammatory agent, an antibiotic, an anti-viral agent, an anti-hypertensive agent, a chemosensitizing agent and a combination thereof.

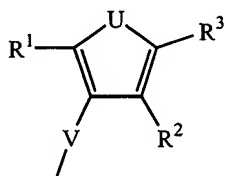
14. (Original) The self-immolative dendrimer of claim 13, wherein said anti-proliferative agent is a chemotherapeutic agent.

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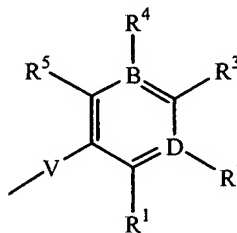
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15. (Currently Amended) The self-immolative dendrimer of claim 12, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a ~~single-signal~~ absorber agent and a combination thereof.

16. (Currently Amended) The self-immolative dendrimer of claim 1, wherein said self-immolative chemical linker has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

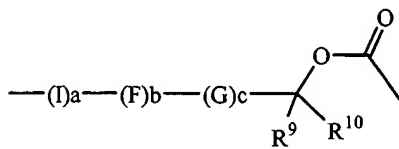
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonoxy or phosphate,

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or alternatively, at least two of R^1 , R^2 , R^3 , R^4 and R^5 being connected to one another to form an aromatic or aliphatic cyclic structure;

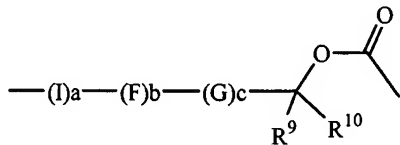
whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently $-R^{11}C=CR^{12}-$ or $-C\equiv C-$, where each of R^{11} and R^{12} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 , ~~and~~ R^8 , R^9 and R^{10} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



17. (Original) The self-immolative dendrimer of claim 16, wherein said self-immolative chemical linker has the general Formula Ib.

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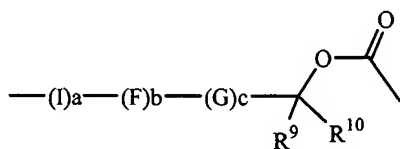
18. (Original) The self-immolative dendrimer of claim 17, wherein:

V is O or S;

each of B and D is a carbon atom;

each of R^2 , R^3 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 and R^5 is said



19. (Original) The self-immolative dendrimer of claim 18, wherein:

each of R^2 , R^3 and R^4 is independently hydrogen or alkyl;

each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

20. (Original) The self-immolative dendrimer of claim 17, wherein

V is O or S;

each of B and D is a carbon atom;

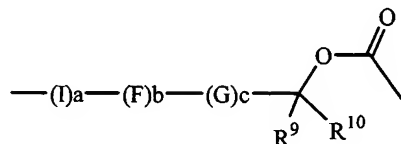
each of R^2 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 , R^3 and R^5 is said



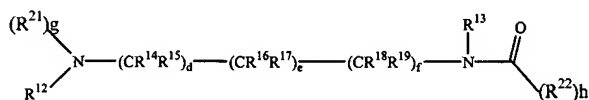
21. (Original) The self-immolative dendrimer of claim 20, wherein:

each of R^2 and R^4 is independently hydrogen or alkyl;

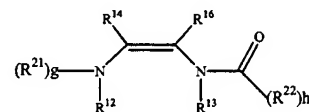
each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

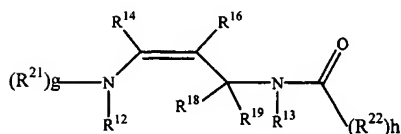
22. (Currently Amended) The self-immolative dendrimer of claim 3, wherein said self-immolative spacer has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc, Formula IId:



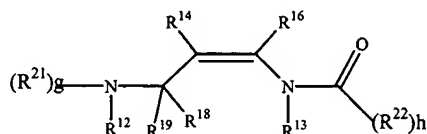
Formula IIa



Formula IIb



Formula IIc



Formula IId

and a combination thereof,

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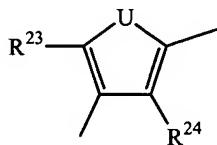
wherein:

d, e, f, g and h are each independently an integer from 0 to 3, provided that $d + e + f \leq 2$;

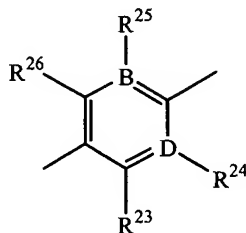
R^{12} and R^{13} are each independently hydrogen, alkyl or cycloalkyl;

R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;

R^{21} and R^{22} each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:



Formula VIIa



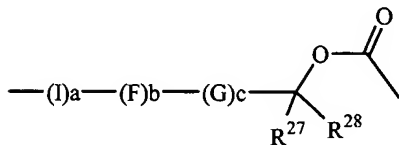
Formula VIIb

wherein:

U is O, S or NR^{29} ;

B and D are each independently a carbon atom or a nitrogen atom;

R^{23} , R^{24} , R^{25} and R^{26} are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy,

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thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^{23} , R^{24} , R^{25} and R^{26} being connected to one another to form an aromatic or aliphatic cyclic structure;

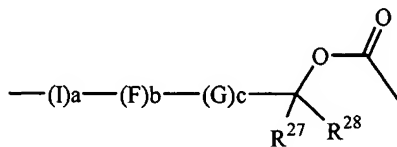
whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently $-R^{30}C=CR^{31}-$ or $-C\equiv C-$, where each of R^{30} and R^{31} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{30} and R^{31} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^{27} , R^{28} and R^{29} is are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^{23} and R^{24} in Formula VIIa and of R^{23} , R^{24} , R^{35} and R^{26} in Formula VIIb are said



23. (Original) The self-immolative dendrimer of claim 22, wherein said self-immolative spacer has the general Formula IIa.

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24. (Original) The self-immolative dendrimer of claim 1, being between a first and a tenth generation dendrimer.

25. (Original) The self-immolative dendrimer of claim 1, having between 2 and 5 ramifications in each generation.

26. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one therapeutically active agent.

27. (Original) The self-immolative dendrimer of claim 26, wherein said at least one therapeutically active agent comprises at least one chemotherapeutic agent.

28. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least two therapeutically active agents.

29. (Original) The self-immolative dendrimer of claim 2, wherein said at least two therapeutically active agents are synergistic.

30. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one diagnostic agent.

31. (Original) The self-immolative dendrimer of claim 30, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a signal absorber agent and a combination thereof.

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32. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is a photo-labile trigger unit and said functional moieties comprise at least one diagnostic agent.

33. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is a hydrolyzable trigger unit and said functional moieties comprise at least one agrochemical.

34. (Original) The self-immolative dendrimer of claim 2, wherein said trigger unit is a chemically removable trigger unit and said functional moieties comprise at least one diagnostic agent.

35-53. (Canceled).

54. (Original) A pharmaceutical composition comprising, as an active ingredient, the self-immolative dendrimer of claim 2 and a pharmaceutically acceptable carrier.

55. (Original) The pharmaceutical composition of claim 54, packaged in a packaging material and identified in print, in or on said packaging material, for use in the treatment of a disease or disorder selected from the group consisting of a proliferative disease or disorder, an inflammatory disease or disorder, a bacterial disease or disorder, a viral disease or disorder and a hypertensive disease or disorder.

56. (Original) The pharmaceutical composition of claim 54, packaged in a packaging material and identified in print, in or on said packaging material, for use in a diagnosis.

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57. (Original) The pharmaceutical composition of claim 54, wherein said self-immolative dendrimer further comprises at least one self-immolative spacer.

58. (Original) The pharmaceutical composition of claim 57, wherein said spacer linking said trigger unit and said at least one self-immolative chemical linker.

59. (Original) The pharmaceutical composition of claim 57, wherein said at least one spacer linking at least one of said functional moieties and at least one of said at least one chemical linker.

60. (Original) The pharmaceutical composition of claim 57, wherein said trigger unit, said at least one spacer and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker and said at least one spacer self-immolate to thereby release said functional moieties

61. (Original) The pharmaceutical composition of claim 54, wherein said cleavable trigger unit is selected from the group consisting of a photo-labile trigger unit, a chemically removable trigger unit, a hydrolizable trigger unit and a biodegradable trigger unit.

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62. (Original) The pharmaceutical composition of claim 61, wherein said biodegradable trigger unit is an enzymatically cleavable trigger unit.

63. (Original) The pharmaceutical composition of claim 54, wherein said functional moieties comprise at least one therapeutically active agent.

64. (Original) The pharmaceutical composition of claim 54, wherein said functional moieties comprise at least two therapeutically active agents.

65. (Original) The pharmaceutical composition of claim 64, wherein said at least two therapeutically active agents are synergistic.

66. (Original) The pharmaceutical composition of claim 54, wherein said functional moieties comprise at least one diagnostic agent.

67. (Original) The pharmaceutical composition of claim 63, wherein said at least one therapeutically active agent is selected from the group consisting of an anti-proliferative agent, an anti-inflammatory agent, an antibiotic, an anti-viral agent, an anti-hypertensive agent, a chemosensitizing agent and a combination thereof.

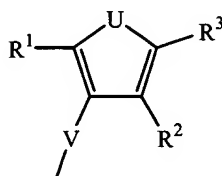
68. (Original) The pharmaceutical composition of claim 67, wherein said anti-proliferative agent is a chemotherapeutic agent.

69. (Currently Amended) The pharmaceutical composition of claim 66, wherein said diagnostic agent is selected from the group consisting of a signal generator agent, a ~~single-signal~~ absorber agent and a combination thereof.

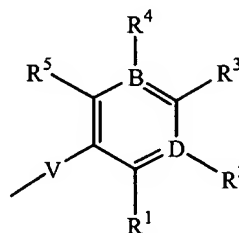
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70. (Currently Amended) The pharmaceutical composition of claim 54, wherein said self-immolative chemical linker has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

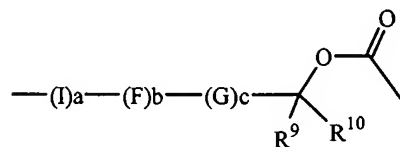
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R¹, R², R³, R⁴ and R⁵ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently -R¹¹C=CR¹²- or -C(T)-, where each of R¹¹ and R¹² is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl,

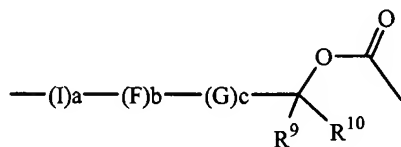
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heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 , R^8 , R^9 and R^{10} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



71. (Original) The pharmaceutical composition of claim 70, wherein said self-immolative chemical linker has the general Formula Ib.

72. (Original) The pharmaceutical composition of claim 71, wherein:

V is O or S;

each of B and D is a carbon atom;

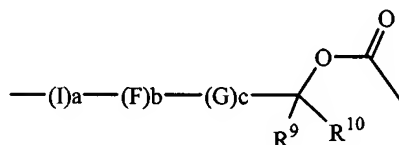
each of R^2 , R^3 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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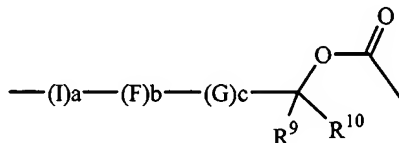
or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 and R^5 is said



73. (Original) The pharmaceutical composition of claim 72, wherein:
 each of R^2 , R^3 and R^4 is independently hydrogen or alkyl;
 each of a, b and c equal 0; and
 each of R^9 and R^{10} is independently hydrogen or alkyl.

74. (Original) The pharmaceutical composition of claim 71, wherein
 V is O or S;
 each of B and D is a carbon atom;
 each of R^2 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and
 each of R^1 , R^3 and R^5 is said



75. (Original) The pharmaceutical composition of claim 74, wherein:

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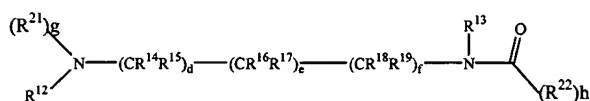
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each of R^2 and R^4 is independently hydrogen or alkyl;

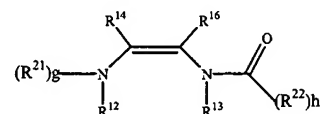
each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

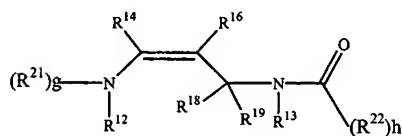
76. (Currently Amended) The pharmaceutical composition of claim 57, wherein said self-immolative spacer has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc and Formula IId:



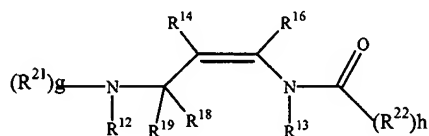
Formula IIa



Formula IIb



Formula IIc



Formula IId

and a combination thereof,

wherein:

d, e, f, g and h and f are each independently an integer from 0 to 3, provided that $d + e + f \leq 2$;

R^{12} and R^{13} are each independently hydrogen or alkyl;

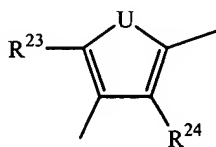
R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy,

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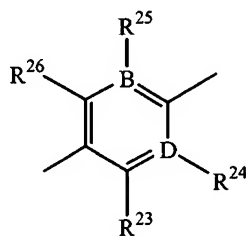
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carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;

R^{21} and R^{22} are each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:



Formula VIIa



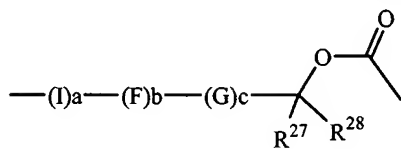
Formula VIIb

wherein:

U is O, S or NR^{29} ;

B and D are each independently a carbon atom or a nitrogen atom;

R^{23} , R^{24} , R^{25} and R^{26} are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^{23} , R^{24} , R^{25} and R^{26} being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

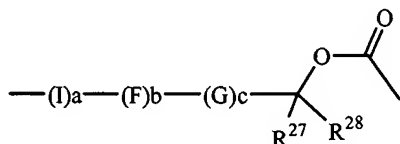
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I, F and G are each independently $-R^{30}C=CR^{31}-$ or $-C\equiv C-$, where each of R^{30} and R^{31} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{30} and R^{31} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^{27} , R^{28} and R^{29} is hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^{23} and R^{24} in Formula VIIa and of R^{23} , R^{24} , R^{35} and R^{26} in Formula VIIb are said



77. (Original) The pharmaceutical composition of claim 76, wherein said self-immolative spacer has the general Formula IIa.

78. (Original) The pharmaceutical composition of claim 54, wherein said self-immolative dendrimer is between a first and a tenth generation dendrimer.

79. (Original) The pharmaceutical composition of claim 54, wherein said self-immolative dendrimer has between 2 and 5 ramifications in each generation.

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80. (Original) The pharmaceutical composition of claim 54, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one therapeutically active agent.

81. (Original) The pharmaceutical composition of claim 80, wherein said at least one therapeutically active agent comprises at least one chemotherapeutic agent.

82. (Original) The pharmaceutical composition of claim 54, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one diagnostic agent.

83. (Currently Amended) The pharmaceutical composition of claim 82, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a signal absorber agent and a combination thereof.-

84-101. (Canceled).

102. (Original) An agricultural composition, comprising, as an active ingredient, the self-immolative dendrimer of claim 33, and an agricultural acceptable carrier.

103. (Withdrawn) A method of treating a disorder or disease selected from the group consisting of a proliferative disease or disorder, an inflammatory disease or disorder, a bacterial disease or disorder, a viral disease or disorder and a hypertensive disease or disorder in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the self-immolative dendrimer of claim 9, 10 or 11.

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104. (Withdrawn) The method of claim 103, wherein said self-immolative dendrimer further comprises at least one self-immolative spacer.

105. (Withdrawn) The method of claim 104, wherein said spacer linking said trigger unit and said at least one self-immolative chemical linker.

106. (Withdrawn) The method of claim 104, wherein said at least one spacer linking at least one of said functional moieties and at least one of said at least one chemical linker.

107. (Withdrawn) The method of claim 104, wherein said trigger unit, said at least one spacer and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker and said at least one spacer self-immolate to thereby release said functional moieties.

108. (Withdrawn) The method of claim 103, wherein said cleavable trigger unit is an enzymatically cleavable trigger unit.

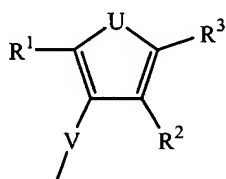
109. (Withdrawn) The method of claim 103, wherein said at least one therapeutically active agent is selected from the group consisting of an anti-proliferative agent, an anti-inflammatory agent, an antibiotic, an anti-viral agent, an anti-hypertensive agent, a chemosensitizing agent and a combination thereof.

110. (Withdrawn) The method of claim 109, wherein said anti-proliferative agent is a chemotherapeutic agent.

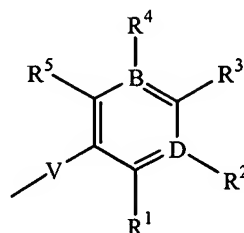
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111. (Withdrawn) The method of claim 103, wherein said self-immolative chemical linker has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

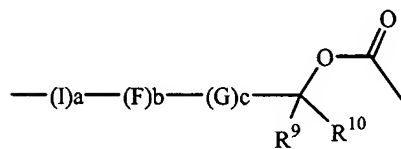
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R¹, R², R³, R⁴ and R⁵ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently -R¹¹C=CR¹²- or -C(T)-, where each of R¹¹ and R¹² is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl,

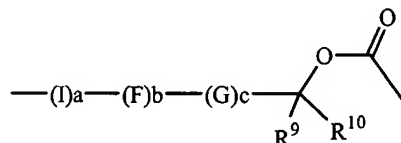
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heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 and R^8 are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



112. (Withdrawn) The method of claim 111, wherein said self-immolative chemical linker has the general Formula Ib.

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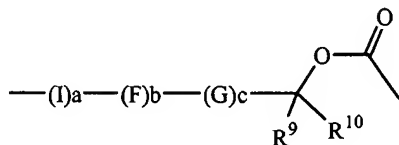
113. (Withdrawn) The method of claim 112, wherein:

V is O or S;

each of B and D is a carbon atom;

each of R^2 , R^3 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 and R^5 is said



114. (Withdrawn) The method of claim 113, wherein:

each of R^2 , R^3 and R^4 is independently hydrogen or alkyl;

each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

115. (Withdrawn) The method of claim 112, wherein

V is O or S;

each of B and D is a carbon atom;

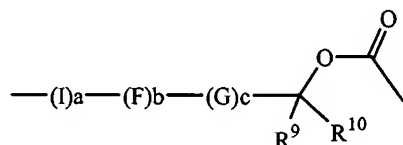
each of R^2 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 , R^3 and R^5 is said



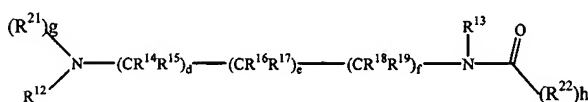
116. (Withdrawn) The method of claim 115, wherein:

each of R^2 and R^4 is independently hydrogen or alkyl;

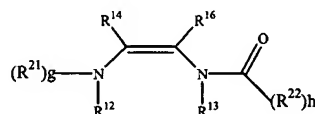
each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

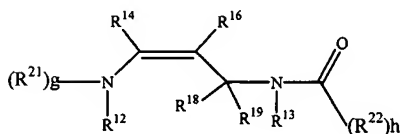
117. (Withdrawn) The method of claim 104, wherein said self-immolative spacer has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc and Formula IId:



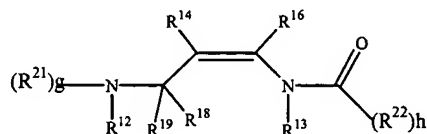
Formula IIa



Formula IIb



Formula IIc



Formula IId

and a combination thereof,

wherein:

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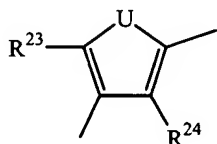
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d, e, f, g and h and f are each independently an integer from 0 to 3, provided that $d + e + f \leq 2$;

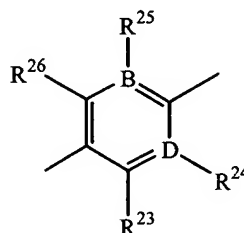
R^{12} and R^{13} are each independently hydrogen or alkyl;

R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;

R^{21} and R^{22} are each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:



Formula VIIa



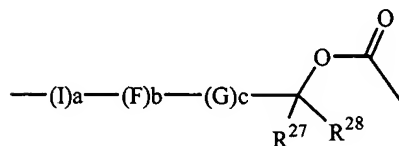
Formula VIIb

wherein:

U is O, S or NR^{29} ;

B and D are each independently a carbon atom or a nitrogen atom;

R^{23} , R^{24} , R^{25} and R^{26} are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate,

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sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^{23} , R^{24} , R^{25} and R^{26} being connected to one another to form an aromatic or aliphatic cyclic structure;

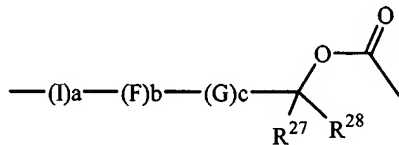
whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently $-R^{30}C=CR^{31}-$ or $-C\equiv C-$, where each of R^{30} and R^{31} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{30} and R^{31} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^{29} is hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^{23} and R^{24} in Formula VIIa and of R^{23} , R^{24} , R^{35} and R^{26} in Formula VIIb are said



118. (Withdrawn) The method of claim 117, wherein said self-immolative spacer has the general Formula IIa.

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119. (Withdrawn) A method of determining a concentration of an enzyme, the method comprising contacting said enzyme with the self-immolative dendrimer of claim 30.

120. (Withdrawn, Previously Presented) The method of claim 119, wherein said contacting is effected *in vitro*.

121. (Withdrawn, Previously Presented) The method of claim 119, wherein said contacting is effected *in vivo*.

122. (Withdrawn) A method of determining a concentration of a chemical reagent, the method comprising contacting said chemical reagent with the self-immolative dendrimer of claim 34.

123. (Withdrawn) A method of synthesizing a first generation self-immolative dendrimer of claim 1, the method comprising:

(a) providing a first compound having said self-immolative chemical linker being linked to said cleavable trigger unit and to at least two first reactive groups; and

(b) coupling said first compound with at least two equivalents of at least one second compound, thereby generating said first generation self-immolative dendrimer of claim 1 having a cleavable trigger unit as its core, at least two residues of said second compound as its tail units and a self-immolative chemical linker linking therebetween.

124. (Withdrawn) The method of claim 123, wherein said self-immolative chemical linker is linked to said cleavable trigger unit via a self-immolative spacer, the method further comprising, prior to (a):

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(c) providing a third compound having said self-immolative chemical linker being linked to said at least two first reactive groups and to a second reactive group;

(d) coupling said third compound with said self-immolative spacer, to thereby provide a forth compound having said self-immolative chemical linker being linked to said at least two first reactive groups and to said self-immolative spacer; and

(e) coupling said forth compound with said cleavable trigger unit, to thereby provide said first compound.

125. (Withdrawn) The method of claim 123, wherein each of said first reactive groups comprises a carbonate group.

126. (Withdrawn) The method of claim 123, wherein said second compound comprises a free amino group.

127. (Withdrawn) The method of claim 123, wherein at least one of said tail units is linked to said chemical linker via a self-immolative spacer, the method further comprising, prior to (b):

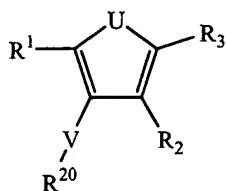
(f) providing at least one second compound having a self-immolative spacer linked thereto.

128. (Withdrawn) The method of claim 124, wherein said second reactive group is selected from the group consisting of a hydroxyl, a thiol and an amine.

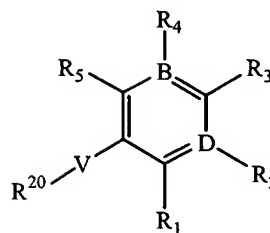
129. (Withdrawn) The method of claim 123, wherein said first compound has a general formula selected from the group consisting of Formula IVa and Formula IVb:

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Formula IVa



Formula IVb

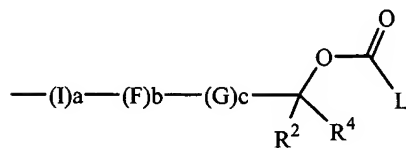
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl,

heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R¹, R², R³, R⁴ and R⁵ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5;

I, F and G are each independently -R¹¹C=CR¹²- or -C≡C-, where each of R¹¹ and R¹² is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate,

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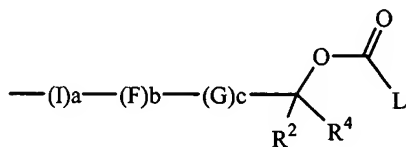
sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

L is a leaving group;

R^6 , R^7 and R^8 are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate; and

R^{20} is said cleavable trigger unit or a self-immolative spacer terminating with said cleavable trigger unit,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



130. (Withdrawn) A method of synthesizing a first generation of the self-immolative dendrimer of claim 1, the method comprising:

- (a) providing a first compound having a self-immolative chemical linker being linked to at least two tail units and to a first reactive group; and
- (b) coupling said first compound with said cleavable trigger unit.

131. (Withdrawn) The method of claim 123, wherein said self-immolative chemical linker is linked to said cleavable trigger unit via a self-immolative spacer, the method further comprising, prior to (b):

- (c) coupling said first compound with said self-immolative spacer.

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132. (Withdrawn) The method of claim 130, wherein each of said tail units is linked to said chemical linker via a carbamate bond.

133. (Withdrawn) The method of claim 132, wherein said tail units are derived from at least one second compound having a free amino group.

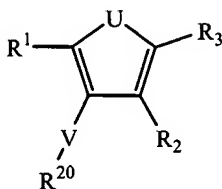
134. (Withdrawn) The method of claim 130, wherein at least one of said tail units is linked to said chemical linker via a self-immolative spacer, the method further comprising, prior to (a):

(f) providing at least one third compound having a self-immolative spacer linked thereto; and

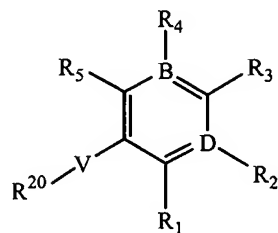
(g) coupling at least two equivalents of said at least one third compound with said self-immolative chemical linker.

135. (Withdrawn) The method of claim 130, wherein said first reactive group is selected from the group consisting of a hydroxyl, a thiol and an amine.

136. (Withdrawn) The method of claim 130, wherein said first compound has a general formula selected from the group consisting of Formula IVa and Formula IVb:



Formula IVa



Formula IVb

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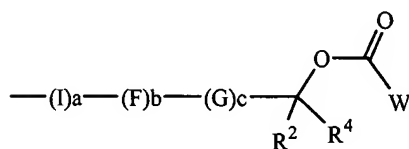
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R¹, R², R³, R⁴ and R⁵ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5;

I, F and G are each independently -R¹¹C=CR¹²- or -C≡C-, where each of R¹¹ and R¹² is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R¹¹ and R¹² being connected to one another to form an aromatic or aliphatic cyclic structure; and

W is one of said at least two tail unit;

R⁶, R⁷ and R⁸ are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate,

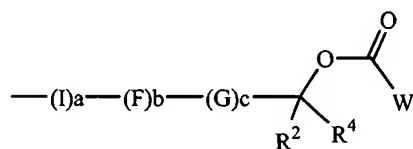
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sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;
 and

R^{20} is hydrogen, alkyl or cycloalkyl,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



137. (Withdrawn) A method of synthesizing a Nth generation self-immolative dendrimer of claim 1, wherein N is an integer greater than 1, the method comprising:

(a) providing a (N-1)th generation self-immolative dendrimer including a first self-immolative chemical linker being linked to a first reactive group, (N-1) (N-1)th self-immolative chemical linkers each being linked to at least two second reactive groups, and a plurality of self-immolative chemical linkers linking therebetween;

(b) providing a Nth compound having a Nth self-immolative chemical linker being linked to a (N+1)th reactive group and to at least two (N+2)th reactive groups;

(c) coupling at least $2(N-1)$ equivalents of said Nth compound to said (N-1)th generation self-immolative dendrimer, to thereby provide a Nth generation self-immolative dendrimer having at least $2N(N+2)$ th reactive groups as its tail units and said first reactive group being linked to said first chemical linker; and

(d) coupling said Nth generation self-immolative dendrimer having at least $2N(N+2)$ th reactive groups as its tail units with at least $2N$ equivalents of at least one (N+1)th compound, to thereby provide said Nth generation self-immolative dendrimer having $2N$ tail units and a first reactive group as its core.

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138. (Withdrawn) The method of claim 137, wherein said first reactive group is said cleavable trigger unit.

139. (Withdrawn) The method of claim 137, wherein said first reactive group is selected from the group consisting of hydroxyl, thiol and amine, the method further comprising, prior to (a) or after (d):

(e) coupling said first reactive group with said cleavable trigger unit.

140. (Withdrawn) The method of claim 138, wherein said first self-immolative chemical linker is linked to said cleavable trigger unit via a self-immolative spacer, the method further comprising, prior to (a):

(f) coupling said first self-immolative chemical linker with said self-immolative spacer.

141. (Withdrawn) The method of claim 139, wherein said first self-immolative chemical linker is linked to said cleavable trigger unit via a self-immolative spacer, the method further comprising, prior to (e):

(g) coupling said first reactive group with said self-immolative spacer.

142. (Withdrawn) The method of claim 137, wherein each of said second and (N+2)th reactive groups comprises a carbonate functional group.

143. (Withdrawn) The method of claim 137, wherein said (N+1)th compound comprises a free amino group.

144. (Withdrawn) The method of claim 137, wherein at least one of said tail units is linked to said chemical linker via a self-immolative spacer, the method further comprising, prior to (d):

(h) providing at least one (N+1)th compound having said self-immolative spacer linked thereto.

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145. (Withdrawn) The method of claim 137, wherein said (N+1)th reactive group is selected from the group consisting of a hydroxyl, a thiol and an amine.

146. (Withdrawn) The method of claim 137, wherein said Nth compound is linked to said (N-1)th generation self-immolative dendrimer via a self-immolative spacer, the method further comprising, prior to (c):

coupling said Nth self-immolative chemical linker with said self-immolative spacer, to thereby provide said Nth compound having said Nth self-immolative chemical linker being linked to said self-immolative spacer and to at least two (N+2)th reactive groups.

147. (Withdrawn) A method of performing a diagnosis, the method comprising administering to the subject a diagnostically effective amount of the self-immolative dendrimer of claim 30.

148. (Withdrawn) The method of claim 147, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a signal absorber agents and a combination thereof.

149. (Withdrawn) The method of claim 147, wherein said self-immolative dendrimer further comprises at least one self-immolative spacer.

150. (Withdrawn) The method of claim 149, wherein said spacer linking said trigger unit and said at least one self-immolative chemical linker.

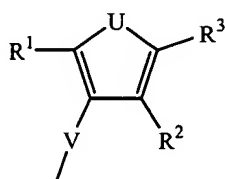
151. (Withdrawn) The method of claim 149, wherein said at least one spacer linking at least one of said functional moieties and at least one of said at least one chemical linker.

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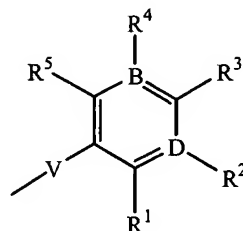
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152. (Withdrawn) The method of claim 149, wherein said trigger unit, said at least one spacer and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker and said at least one spacer self-immolate to thereby release said functional moieties.

153. (Withdrawn) The method of claim 147, wherein said self-immolative chemical linker has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

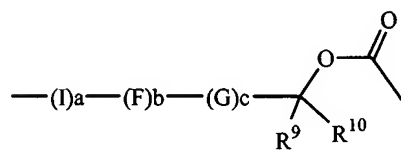
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic

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alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^1 , R^2 , R^3 , R^4 and R^5 being connected to one another to form an aromatic or aliphatic cyclic structure;

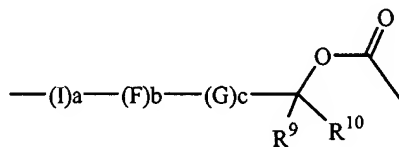
whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently $-R^{11}C=CR^{12}-$ or $-C\equiv C-$, where each of R^{11} and R^{12} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 and R^8 are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



154. (Withdrawn) The method of claim 153, wherein said self-immolative chemical linker has the general Formula Ib.

155. (Withdrawn) The method of claim 154, wherein:

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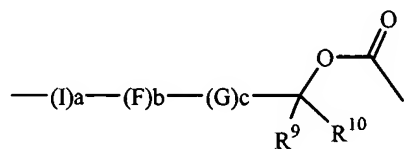
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V is O or S;

each of B and D is a carbon atom;

each of R^2 , R^3 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 and R^5 is said



156. (Withdrawn) The method of claim 155, wherein:
 each of R^2 , R^3 and R^4 is independently hydrogen or alkyl;
 each of a, b and c equal 0; and
 each of R^9 and R^{10} is independently hydrogen or alkyl.

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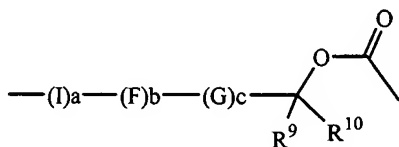
157. (Withdrawn) The method of claim 154, wherein

V is O or S;

each of B and D is a carbon atom;

each of R^2 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 , R^3 and R^5 is said



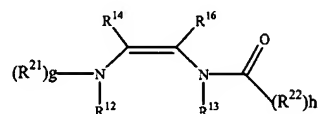
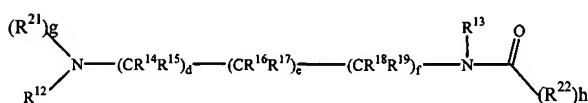
158. (Withdrawn) The method of claim 157, wherein:

each of R^2 and R^4 is independently hydrogen or alkyl;

each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

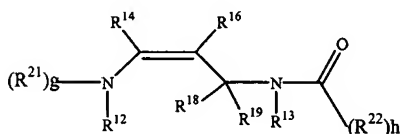
159. (Withdrawn) The method of claim 149, wherein said self-immolative spacer has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc and Formula IId:



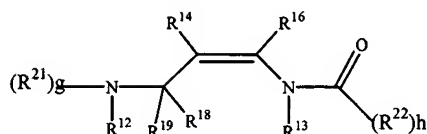
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Formula IIa



Formula IIb



Formula IIc

Formula IIId

and a combination thereof,

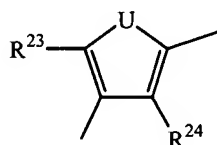
wherein:

d, e, f, g and h and f are each independently an integer from 0 to 3, provided that $d + e + f \leq 2$;

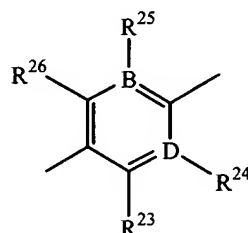
R^{12} and R^{13} are each independently hydrogen or alkyl;

R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;

R^{21} and R^{22} are each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:



Formula VIIa



Formula VIIb

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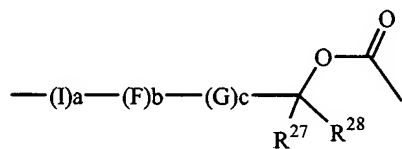
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wherein:

U is O, S or NR²⁹;

B and D are each independently a carbon atom or a nitrogen atom;

R²³, R²⁴, R²⁵ and R²⁶ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R²³, R²⁴, R²⁵ and R²⁶ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

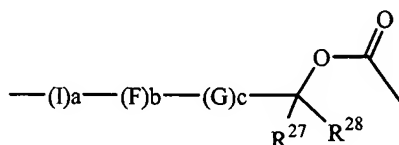
I, F and G are each independently $\text{---R}^{30}\text{C=CR}^{31}\text{---}$ or $\text{---C}\equiv\text{C---}$, where each of R³⁰ and R³¹ is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R³⁰ and R³¹ being connected to one another to form an aromatic or aliphatic cyclic structure; and

R²⁹ is hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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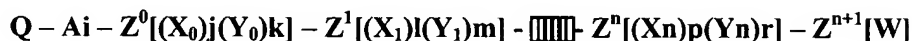
provided that at least two of R^{23} and R^{24} in Formula VIIa and of R^{23} , R^{24} , R^{35} and R^{26} in Formula VIIb are said



160. (Withdrawn) The method of claim 159, wherein said self-immolative spacer has the general Formula IIa.

161. (Original) A self-immolative dendrimer.

162. (Previously Presented) The self-immolative dendrimer of claim 1, having a general Formula III:



Formula III

wherein:

n is an integer from 0 to 10, representing the generation number of the dendrimer;

each of i , j , k , l , m , p and r is independently an integer of 0 to 10;

Q is said cleavable trigger unit;

A is a first self-immolative spacer linking said trigger unit and said self-immolative linker, or absent (when i is 0);

Z is an integer of between 2 and 5, representing the ramification number of the dendrimer;

X is said self-immolative chemical linker;

Y is a second self-immolative spacer linking said self-immolative linker and said tail units, or absent (when k , m or r is 0); and

W is a tail unit in said plurality of said tail units,

whereas, when n equals 0, each of l , m , p and r equals 0; and

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when n equals 1, each of p and r equals 0.

163. (Previously Presented) The self-immolative dendrimer of claim 162, wherein said $Z^{n+1}[W]$ comprise at least two functional moieties, said functional moieties being the same or different.

164. (Previously Presented) The self-immolative dendrimer of claim 162, wherein Z equals 2 or 3.

165. (Previously Presented) The self-immolative dendrimer of claim 162, wherein said cleavable trigger unit Q is selected from the group consisting of a photolabile trigger unit, a chemically removable trigger unit, a hydrolyzable trigger unit and a biodegradable trigger unit.

166. (Previously Presented) The self-immolative dendrimer of claim 165, wherein said biodegradable trigger unit is an enzymatically cleavable trigger unit.

167. (Previously Presented) The self-immolative dendrimer of claim 163, wherein said tail units W comprise at least one therapeutically active agent.

168. (Previously Presented) The self-immolative dendrimer of claim 163, wherein said tail units W comprise at least one diagnostic agent.

169. (Previously Presented) The self-immolative dendrimer of claim 167, wherein said at least one therapeutically active agent is selected from the group consisting of an anti-proliferative agent, an anti-inflammatory agent, an antibiotic, an anti-viral agent, an anti-hypertensive agent and combinations thereof.

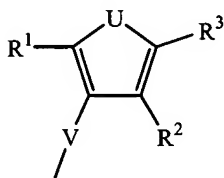
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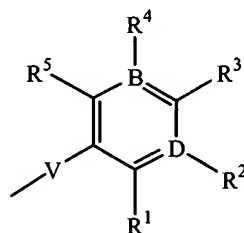
170. (Previously Presented) The self-immolative dendrimer of claim 169, wherein said anti-proliferative agent is a chemotherapeutic agent.

171. (Currently Amended) The self-immolative dendrimer of claim 168, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a ~~single-signal~~ absorber agent and a combination thereof.

172. (Currently Amended) The self-immolative dendrimer of claim 162, wherein each of said self-immolative chemical linkers X_0 - X_n independently has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

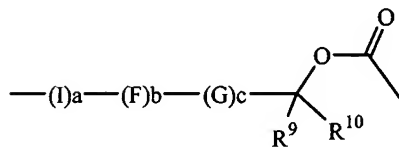
wherein:

V is O, S, PR^6 or NR^7 ;

U is O, S or NR^8 ;

B and D are each independently a carbon atom or a nitrogen atom;

R^1 , R^2 , R^3 , R^4 and R^5 are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonoxy or phosphate, or alternatively, at

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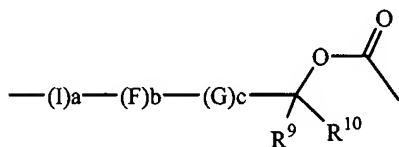
least two of R^1 , R^2 , R^3 , R^4 and R^5 being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently $-R^{11}C=CR^{12}-$ or $-C\equiv C-$, where each of R^{11} and R^{12} is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 , ~~and R^8~~ , R^9 and R^{10} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



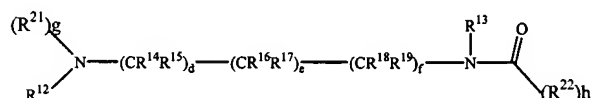
173. (Previously Presented) The self-immolative dendrimer of claim 172, wherein each of said self-immolative chemical linkers X_0 - X_n has the general Formula Ib.

174. (Currently Amended) The self-immolative dendrimer of claim 162, wherein each of said first self-immolative spacer A and said self-immolative spacers

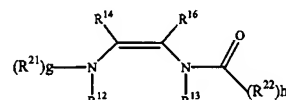
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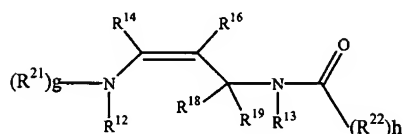
Y_0 - Y_n independently has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc and Formula IId:



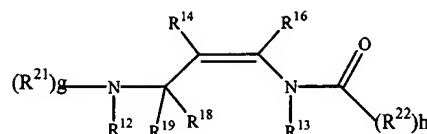
Formula IIa



Formula IIb



Formula IIc



Formula IId

and a combination thereof,

wherein:

d, e, f, g and h and f are each independently an integer from 0 to 3, provided that $d + e + f \geq 2$;

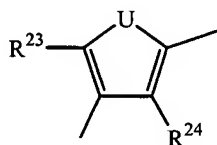
R^{12} and R^{13} are each independently hydrogen or alkyl;

R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonoxy or phosphate;

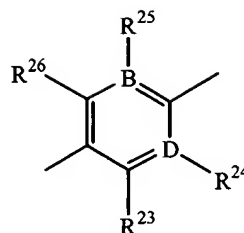
R^{21} and R^{22} are each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:

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Formula VIIa



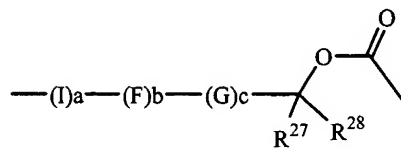
Formula VIIb

wherein:

U is O, S or NR²⁹;

B and D are each independently a carbon atom or a nitrogen atom;

R²³, R²⁴, R²⁵ and R²⁶ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl,

heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R²³, R²⁴, R²⁵ and R²⁶ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently -R³⁰C=CR³¹- or -C≡C-, where each of R³⁰ and R³¹ is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R³⁰

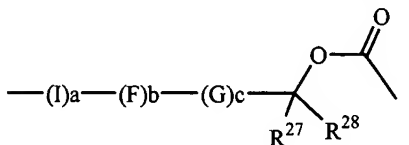
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and R³¹ being connected to one another to form an aromatic or aliphatic cyclic structure; and

R²⁷, R²⁸ and R²⁹ is are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R²³ and R²⁴ in Formula VIIa and of R²³, R²⁴, R³⁵ and R²⁶ in Formula VIIb are said



175. (Previously Presented) The self-immolative dendrimer of claim 174, wherein each of said first self-immolative spacer A and said self-immolative spacers Y₀-Y_n independently has the general Formula IIa.

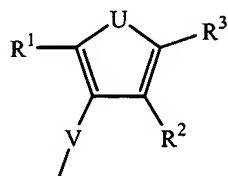
176. (New) A pharmaceutical composition comprising, as an active ingredient, the self-immolative dendrimer of claim 167 and a pharmaceutically acceptable carrier.

177. (New) A self-immolative dendrimer comprising a cleavable trigger unit, a plurality of tail units and at least one self-immolative chemical linker linking between said trigger unit and said tail units, said trigger unit and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker self-immolates, thereby simultaneously releasing all of said tail units,

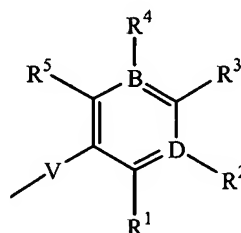
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wherein each said at least one self-immolative chemical linker independently has a general formula selected from the group consisting of Formula Ia and Formula Ib:



Formula Ia



Formula Ib

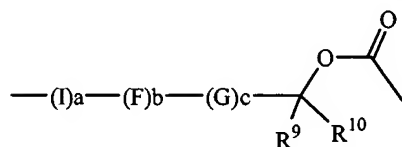
wherein:

V is O, S, PR⁶ or NR⁷;

U is O, S or NR⁸;

B and D are each independently a carbon atom or a nitrogen atom;

R¹, R², R³, R⁴ and R⁵ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R¹, R², R³, R⁴ and R⁵ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

I, F and G are each independently -R¹¹C=CR¹²- or -C(C)-, where each of R¹¹ and R¹² is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino,

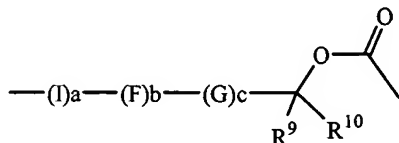
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nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R^{11} and R^{12} being connected to one another to form an aromatic or aliphatic cyclic structure; and

R^6 , R^7 , R^8 , R^9 and R^{10} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

provided that at least two of R^1 , R^2 and R^3 in Formula Ia and of R^1 , R^2 , R^3 , R^4 and R^5 in Formula Ib are said



178. (New) The self-immolative dendrimer of claim 177, wherein said self-immolative chemical linker has the general Formula Ib.

179. (New) The self-immolative dendrimer of claim 178, wherein:

V is O or S;

each of B and D is a carbon atom;

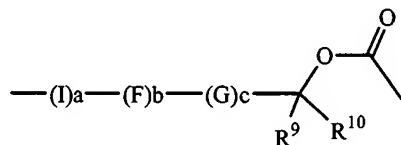
each of R^2 , R^3 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 and R^5 is said



180. (New) The self-immolative dendrimer of claim 179, wherein:

each of R^2 , R^3 and R^4 is independently hydrogen or alkyl;

each of a, b and c equal 0; and

each of R^9 and R^{10} is independently hydrogen or alkyl.

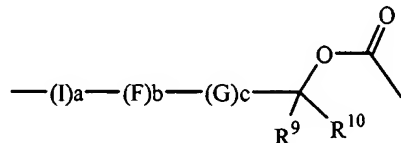
181. (New) The self-immolative dendrimer of claim 178, wherein

V is O or S;

each of B and D is a carbon atom;

each of R^2 and R^4 is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R^2 , R^3 and R^4 being connected to one another to form an aromatic or aliphatic cyclic structure; and

each of R^1 , R^3 and R^5 is said



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182. (New) The self-immolative dendrimer of claim 181, wherein:
 each of R^2 and R^4 is independently hydrogen or alkyl;
 each of a, b and c equal 0; and
 each of R^9 and R^{10} is independently hydrogen or alkyl.

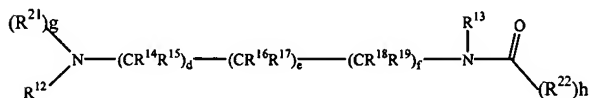
183. (New) The self-immolative dendrimer of claim 177, further comprising at least one self-immolative spacer.

184. (New) The self-immolative dendrimer of claim 183, wherein said spacer linking said trigger unit and said at least one self-immolative chemical linker.

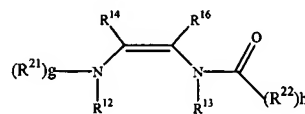
185. (New) The self-immolative dendrimer of claim 183, wherein said at least one spacer linking at least one of said tail units and at least one of said at least one chemical linker.

186. (New) The self-immolative dendrimer of claim 183, wherein said trigger unit, said at least one spacer and said at least one self-immolative chemical linker being such that upon cleavage of said trigger unit, said at least one self-immolative chemical linker and said at least one spacer self-immolate to thereby release said tail units.

187. (New) The self-immolative dendrimer of claim 183, wherein said self-immolative spacer has a general formula selected from the group consisting of Formula IIa, Formula IIb, Formula IIc, Formula IId:



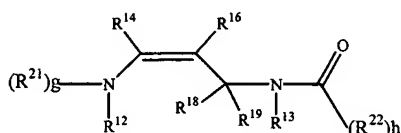
Formula IIa



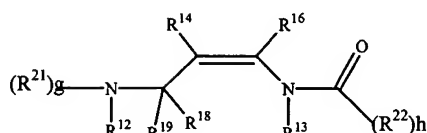
Formula IIb

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Formula IIc



Formula IIId

and a combination thereof,

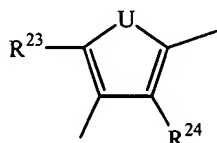
wherein:

d, e, f, g and h are each independently an integer from 0 to 3, provided that $d + e + f \leq 2$;

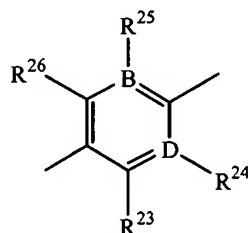
R^{12} and R^{13} are each independently hydrogen, alkyl or cycloalkyl;

R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate;

R^{21} and R^{22} each independently has a general formula selected from the group consisting of Formula VIIa and Formula VIIb:



Formula VIIa



Formula VIIb

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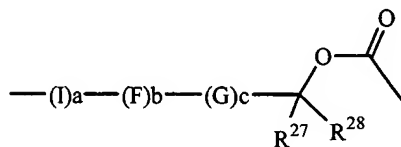
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wherein:

U is O, S or NR²⁹;

B and D are each independently a carbon atom or a nitrogen atom;

R²³, R²⁴, R²⁵ and R²⁶ are each independently



, hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or alternatively, at least two of R²³, R²⁴, R²⁵ and R²⁶ being connected to one another to form an aromatic or aliphatic cyclic structure;

whereas:

a, b and c are each independently as integer of 0 to 5; and

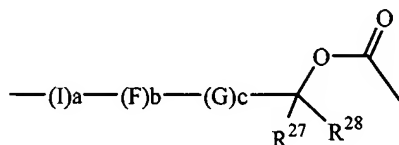
I, F and G are each independently —R³⁰C=CR³¹— or —C(T)—, where each of R³⁰ and R³¹ is independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate, or, alternatively, R³⁰ and R³¹ being connected to one another to form an aromatic or aliphatic cyclic structure; and

R²⁷, R²⁸ and R²⁹ are each independently hydrogen, alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroaryl, alkoxy, hydroxy, thiohydroxy, thioalkoxy, aryloxy, thioaryloxy, amino, nitro, halo, trihalomethyl, cyano, C-amido, N-amido, cyclic alkylamino, imidazolyl, alkylpiperazinyl, morpholino, tetrazole, carboxy, carboxylate, sulfoxy, sulfonate, sulfonyl, sulfixy, sulfinate, sulfinyl, phosphonooxy or phosphate,

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provided that at least two of R^{23} and R^{24} in Formula VIIa and of R^{23} , R^{24} , R^{35} and R^{26} in Formula VIIb are said



188. (New) The self-immolative dendrimer of claim 187, wherein said self-immolative spacer has the general Formula IIa.

189. (New) The self-immolative dendrimer of claim 177, wherein said tail units comprise at least two functional moieties, said at least two functional moieties being the same or different.

190. (New) The self-immolative dendrimer of claim 177, wherein said cleavable trigger unit is selected from the group consisting of a photo-labile trigger unit, a chemically removable trigger unit, a hydrolysable trigger unit and a biodegradable trigger unit.

191. (New) The self-immolative dendrimer of claim 190, wherein said biodegradable trigger unit is an enzymatically cleavable trigger unit.

192. (New) The self-immolative dendrimer of claim 189, wherein said functional moieties comprise at least one therapeutically active agent.

193. (New) The self-immolative dendrimer of claim 189, wherein said functional moieties comprise at least two therapeutically active agents.

194. (New) The self-immolative dendrimer of claim 189, wherein said at least two therapeutically active agents are synergistic.

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195. (New) The self-immolative dendrimer of claim 189, wherein said functional moieties comprise at least one diagnostic agent.

196. (New) The self-immolative dendrimer of claim 192, wherein each of said therapeutically active agents is selected from the group consisting of an anti-proliferative agent, an anti-inflammatory agent, an antibiotic, an anti-viral agent, an anti-hypertensive agent, a chemosensitizing agent and a combination thereof.

197. (New) The self-immolative dendrimer of claim 195, wherein said at least one diagnostic agent is selected from the group consisting of a signal generator agent, a signal absorber agent and a combination thereof.

198. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one therapeutically active agent.

199. (New) The self-immolative dendrimer of claim 198, wherein said at least one therapeutically active agent comprises at least one chemotherapeutic agent.

200. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least two therapeutically active agents.

201. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is an enzymatically cleavable trigger unit and said functional moieties comprise at least one diagnostic agent.

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202. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is a photo-labile trigger unit and said functional moieties comprise at least one diagnostic agent.

203. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is a hydrolyzable trigger unit and said functional moieties comprise at least one agrochemical.

204. (New) The self-immolative dendrimer of claim 189, wherein said trigger unit is a chemically removable trigger unit and said functional moieties comprise at least one diagnostic agent.

205. (New) A pharmaceutical composition comprising the self-immolative dendrimer of claim 189 and a pharmaceutically acceptable carrier.